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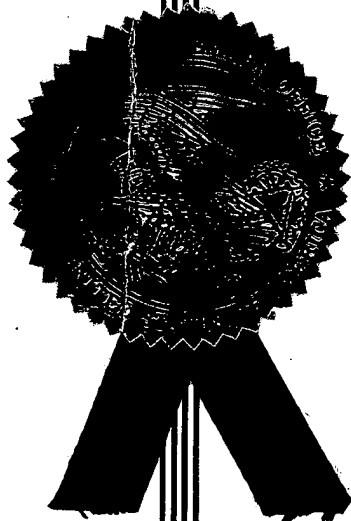
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A-677

U.S. Pat. No. 4,816,484

The  
United  
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The Commissioner of Patents  
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*Has received an application for a patent  
for a new and useful invention. The title  
and description of the invention are en-  
closed. The requirements of law have  
been complied with, and it has been de-  
termined that a patent on the invention  
shall be granted under the law.*

*Therefore, this*

United States Patent

*Grants to the person or persons having  
title to this patent the right to exclude  
others from making, using or selling the  
invention throughout the United States  
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*Donald D. Higgins*

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## NOTICE

*If the application for this patent was filed on or after December 12, 1980, maintenance fees are due three years and six months, seven years and six months, and eleven years and six months after the date of this grant, or within a grace period of six months thereafter upon payment of a surcharge as provided by law. The amount, number, and timing of the maintenance fees required may be changed by law or regulation.*

**United States Patent** [19]  
**Toyoshima et al.**

[11] **Patent Number:** 4,816,484  
[45] **Date of Patent:** Mar. 28, 1989

[54] **HYPOGLYCEMIC AGENT**

[75] **Inventors:** Shigeshi Toyoshima; Yoshiko Seto, both of Funabashi; Hisashi Shinkai, Kawasaki; Koji Toi, Kanagawa; Izumi Kumashiro, Yokohama, all of Japan

[73] **Assignee:** Ajinomoto Co., Inc., Tokyo, Japan

[21] **Appl. No.:** 146,719

[22] **Filed:** Jan. 21, 1988

**Related U.S. Application Data**

[62] Division of Ser. No. 844,970, Mar. 27, 1986, abandoned.

[30] **Foreign Application Priority Data**

Mar. 27, 1985 [JP] Japan ..... 60-62276

[51] **Int. Cl.<sup>4</sup>** ..... A61K 31/215; C07C 101/72

[52] **U.S. Cl.** ..... 514/563; 514/529; 514/530; 549/304; 549/467; 562/445; 562/450; 560/40; 560/41; 546/169; 546/323

[58] **Field of Search** ..... 514/563, 613; 562/445; 560/40

[56] **References Cited**

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2102412 2/1983 United Kingdom .

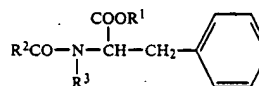
**OTHER PUBLICATIONS**

Toyoshima et al., "Preparation of D-Phenylalanine Derivatives and Their Use as Hypoglycemic Agents", CA 106 85057d (1987).  
European Search Report/Application No. 86 30 2217/26-11-1987.

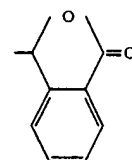
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*Attorney, Agent, or Firm*—Oblon, Fisher, Spivak, McClelland & Maier

[57] **ABSTRACT**

A compound of D-phenylalanine derivative for hypoglycemic use, represented by the general formula



$R^1$  is selected from hydrogen, alkyl of 1 to 5 carbon atoms, aryl of 6 to 12 carbon atoms, aralkyl of 6 to 12 carbon atoms,



$-CH_2CO_2R^3$ ,  $-CH(CH_3)-OCO-R^3$ , and  $-CH_2-OCO-C(CH_3)_3$ ;  $R^2$  is selected from groups comprising aryl of 6 to 12 carbon atoms, a hetero six-membered ring, a hetero five-membered ring, cycloalkyl, or cycloalkenyl, any of which groups may have one or more substituents; and  $R^3$  is selected from hydrogen and alkyl of 1 to 5 carbon atoms; the salts thereof, and precursors which can be converted thereto in the human or animal body.

Some of the compounds are novel per se.

**15 Claims, No Drawings**